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October 19, 1992

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Attn: Section 8(e) Coordinator (CAP Agreement)

Subject: 8ECAP-0024

Dear Section 8(e) Coordinator:

Enclosed are the original and two copies of a study CIBA-GEIGY Corporation is submitting pursuant to the TSCA Section 8(e) Compliance Audit Program and CAP Agreement number 8E CAP-0024. The information being submitted is not considered Confidential Business Information. We are submitting the following information, as required by the CAP Agreement:

Company Name,
Address and

Telephone No.: CIBA-GEIGY Corporation
Attn.: Mr. Anthony Di Battista
Toxicology, Regulatory Auditing and Compliance Dept.
444 Saw Mill River Road
Ardsley, New York 10502-2699

Tel. No. 914-479-2776

Tested Chemical: Exact composition not known. Primary ingredient is lead sulfochromate.

(Primrose Chrome Yellow)

CAS Registry No.: 1344-37-2

Title: Report to Dry Color Manufacturers' Association - 90 day subacute oral toxicity study with Primrose Chrome Yellow in albino rats, December 30, 1975.

Summary: In this study, rats were fed dietary concentrations of 2,000, 5,000 or 20,000 ppm.

Treatment-related findings included reduced hemoglobin and hematocrit values, as well as abnormal erythrocyte morphology. Histopathology revealed treatment-related renal effects, which included lesions, focal interstitial lymphocytic cell infiltrations and chronic nephritis.

3/27/95

Section 8(e) Coordinator
October 19, 1992
Page 2

Category: Unit II.B.2.b.

Prior Reporting: Not applicable

Please call the undersigned at telephone number 302-633-2060 if you have any questions about this submittal.

Very truly yours,

Eva Vary |kf

Eva Vary
Director, Product Safety
Pigments Division

Enclosure: (Two additional copies of this letter and three copies of the submitted study)

cc: A. Di Battista (with cover page of enclosure)

TM - #11396

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Industrial BIO-TEST Laboratories, Inc.

I.D. #

11396

REPORT TO
DRY COLOR MANUFACTURERS' ASSOCIATION
90-DAY SUBACUTE ORAL TOXICITY STUDY WITH
PRIMROSE CHROME YELLOW
IN ALBINO RATS

DECEMBER 30, 1975

IBT NO. 622-05921C

I. Introduction

A sample identified as Primrose Chrome Yellow was received from Dry Color Manufacturers' Association for the purpose of conducting a 90-day subacute oral toxicity study using the albino rat as the test species. A sample identified as White Lead (lead carbonate) was also received and served as a positive control (PC) because of its known toxicologic effect. This report presents the results of the investigation.

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II. Summary

A 90-day subacute oral toxicity study was conducted in which groups of albino rats were fed dietary concentrations of 2,000, 5,000, or 20,000 parts of Primrose Chrome Yellow per million parts of diet. Equivalent concentrations of lead carbonate were fed to groups of animals which served as a positive control. Two groups of animals served as the controls for the study. The following results were obtained during the investigation:

A. Body Weights

Slight to moderate body weight gain suppressions were noted among animals fed either 5,000 or 20,000 ppm lead carbonate. Body weight gains for animals fed 2,000 ppm lead carbonate were not significantly different from those of the control groups. Body weight gains for animals fed 20,000 ppm Primrose Chrome Yellow were slightly to moderately lower than controls. Animals fed 2,000 or 5,000 ppm Primrose Chrome Yellow displayed body weight gains that were comparable to those of the control groups.

B. Food Consumption

The food intake of the males fed 5,000 or 20,000 ppm lead carbonate was somewhat lower (-12% and -19%, respectively) when compared to that of the control groups. Females fed 5,000 or 20,000 ppm and males and females fed 2,000 ppm lead carbonate consumed amounts of food considered comparable to those of the controls. The feeding of Primrose Chrome Yellow at 20,000 ppm caused slightly lower food consumption (-10%) among the males when compared to that of the controls. The food intake of the females fed 20,000 ppm and of the males and females fed 2,000 or 5,000 ppm Primrose Chrome Yellow compared favorably to that of the controls.

C. Mortalities and Reactions

A number of animals fed either 20,000 ppm lead carbonate (1 male, 9 females) or 20,000 ppm Primrose Chrome Yellow (1 male, 3 females) died as a result of trauma incurred at the time of blood collection. The large number of mortalities seemed to indicate the animals were less able to tolerate the stress of blood collection. One female fed 2,000 ppm lead carbonate and 1 female fed the same concentration of Primrose Chrome Yellow also died as a result of trauma at blood collection.

No untoward behavioral reactions were noted during the investigation.

D. Hematologic Studies

No treatment-related effects were noted among animals fed either lead carbonate or Primrose Chrome Yellow in the following parameters:

- total leukocyte count
- erythrocyte count
- neutrophils
- lymphocytes
- monocytes
- eosinophils
- basophils

Treatment-related findings were noted in the following:

- hemoglobin concentration (decrease)
- hematocrit value (decrease)
- mean corpuscular volume (decrease)
- mean corpuscular hemoglobin (decrease)
- mean corpuscular hemoglobin concentration (decrease)
- erythrocyte morphology - size, shape, and color

These findings were noted among the animals fed 5,000 or 20,000 ppm of either lead carbonate or Primrose Chrome Yellow. Values were altered more significantly in males than females. Hematocrit and hemoglobin values were only slightly reduced (not significantly) among the 2,000 ppm animals (PC-1 and T-1), the remaining parameters at this level were not significantly altered by the test material.

E. Blood Chemistry

Slight increases were noted in the serum alkaline phosphatase activity among animals fed 20,000 ppm Primrose Chrome Yellow. Values at the lower 2,000 and 5,000 ppm levels were not statistically different from the controls. Values for the remaining parameters were within the normal ranges for animals of this age and strain.

F. Urinalyses

The routine urinalyses revealed no treatment-related differences for values of the positive control or test animals when compared with the controls. However, increases in the aminolevulinic acid concentrations were noted at all levels of lead carbonate and Primrose Chrome Yellow. The increases occurred in a dose-related manner.

G. Blood Lead Determinations

Blood lead concentrations were elevated in all positive control (lead carbonate) and test animals (Primrose Chrome Yellow) in a dose-related manner. Values among animals fed lead carbonate were considerably higher than those at similar dietary levels of Primrose Chrome Yellow.

H. Gross Pathologic Findings

The findings noted upon gross pathologic examination were similar for control, positive control, and test animals.

I. Organ Weights and Ratios

Slight increases in kidney weights and ratios were observed in all of the positive control groups fed lead carbonate. The females fed 5,000 ppm and

the males and females fed 20,000 ppm of lead carbonate exhibited increased spleen weights and ratios. The animals fed 5,000 ppm or 20,000 ppm Primrose Chrome Yellow exhibited slight increases in kidney weight and kidney to body weight ratios. No differences in kidney weights and ratios were noted between the control animals and the animals fed 2,000 ppm Primrose Chrome Yellow. There were no other changes in organ weights and ratios which could be directly related to the ingestion of either lead carbonate or Primrose Chrome Yellow.

J. Tissue Analyses

The lead content of the bone, brain, kidney, and liver tissues was significantly increased in all animals fed either lead carbonate or Primrose Chrome Yellow. The lead content was increased in a dose-related manner.

The chromium content of the bone, brain, kidney, and liver tissues was not significantly altered by the ingestion of lead carbonate. Brain chromium content was increased among males fed 2,000 or 20,000 ppm Primrose Chrome Yellow. A slight increase was also noted among females fed 20,000 ppm. The bone chromium content was increased among all groups of males fed Primrose Chrome Yellow and among females fed either 5,000 or 20,000 ppm. Kidney and liver chromium content was increased in all groups fed Primrose Chrome Yellow. The increases in chromium content were generally dose-related.

K. Histopathologic Findings

Treatment-related renal lesions consisting of alterations involving tubular epithelial cells were noted among almost all animals of the 3 positive control groups. The changes were confined to the tubules of the mid and inner cortex and consisted of 1) hypertrophy of the epithelial cells and

intranuclear inclusions, 2) desquamation of cells, and 3) increased numbers of mitotic figures. The relative severity was most severe among animals fed 20,000 ppm lead carbonate. Similar treatment-related lesions (with the exception of the increased numbers of mitotic figures) were evident in almost all animals fed Primrose Chrome Yellow. The alterations were not as severe as noted in animals fed comparable levels of lead carbonate.

The other treatment-related renal effects consisted of focal interstitial lymphocytic cell infiltrations and chronic nephritis. These changes were present among the untreated control, positive control and test animals. In the untreated control groups, focal interstitial lymphocytic cell infiltrations were often located unilaterally and were unrelated to the treatment-related tubular changes described above. Among almost all of the positive control animals and most of the T-III animals, focal interstitial lymphocytic cell infiltrations were often located bilaterally and were associated with the treatment-related tubular changes described above. Although chronic nephritis was present among control, positive control, and test animals, the highest incidence occurred among the animals fed 20,000 ppm lead carbonate. The increased incidence and location of chronic nephritis among the animals fed 20,000 ppm lead carbonate was associated with the more severe tubular changes observed among this group of animals.

No treatment-related lesions were noted among the remaining organs and tissues from either the positive control animals or the animals fed Primrose Chrome Yellow.

Respectfully submitted,

INDUSTRIAL BIO-TEST LABORATORIES, INC.

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III. Procedure

A. Experimental Animals

The animals employed in the study were Charles River strain* albino rats. Three hundred twenty rats (160 males and 160 females) were received at this laboratory at 21 days of age. The rats were adapted to the caging and demand-operated water system. After a 14 day acclimation period, the animals were divided into 8 groups and assigned randomly to both group and cage position. Feeding of the test material was initiated when the animals were 35 days of age. Animals were housed individually in standard, wire-bottomed, steel cages. Each cage bore a color-coded card identifying the animal with respect to project number, dietary level assignment, individual animal number, and sex.

B. Organization of Groups

A structural outline of the experiment is shown in Table I.

* Charles River Breeding Laboratories, Inc., Wilmington, Massachusetts.

TABLE I

TEST MATERIAL: Primrose Chrome Yellow
90-Day Subacute Oral Toxicity Study - Albino Rats

Outline of Experiment

Group	Number of Animals		Dietary Level (ppm)
	Males	Females	
Control I	20	20	0
Control II	20	20	0
PC-I	20	20	2,000*
PC-II	20	20	5,000*
PC-III	20	20	20,000*
T-I	20	20	2,000
T-II	20	20	5,000
T-III	20	20	20,000

* Lead Carbonate

C. Body Weights

Each animal used in the study was weighed on the first day of the test and at weekly intervals thereafter. The weights were recorded and served as an index to growth. All body weight data were subjected to statistical analyses.

D. Test Material and Diet Preparation

The diet for the test groups was prepared by blending the appropriate amount of Primrose Chrome Yellow with standard rat ration* in a high-speed blending apparatus. Fresh diets were prepared each week. Each rat was offered an amount of diet sufficient for 1 week's ad libitum feeding. However, checks were made daily to ensure that food was available at all times. The same procedure was repeated for the positive control groups which contained equivalent concentrations of lead carbonate as in the test diets.

The rat chow used in the study was received as 1 single lot in order to eliminate variation in lead content between lots. Ten samples were randomly selected from this lot and analyzed in duplicate to obtain baseline lead values. The following results were obtained:

* Purina Rat Chow (dry, pulverized diet), Ralston-Purina Company, St. Louis, Missouri.

<u>Sample</u>	<u>Lead Content (ppm)</u>
1	0.46, 0.47
2	0.54, 0.54
3	0.61, 0.67
4	0.58, 0.64
5	0.61, 0.52
6	0.67, 0.59
7	0.54, 0.46
8	0.52, 0.52
9	0.47, 0.32
10	0.65, 0.68

The mean lead content on the standard stock ratio was 0.55 ± 0.04 ppm.

E. Food Consumption Data

Food consumption data were collected individually from 5 rats of each sex in each group weekly during the study.

F. Mortality and Reactions

Observations for abnormal reactions and/or deaths were recorded daily during the investigation.

G. Hematologic, Clinical Blood Chemistry Studies and Urinalyses

Blood and urine samples were collected individually from 20 male and 20 female control rats at 0-day, from 10 male and 10 female rats in Control-I, Control-II, PC-III and T-III at 30 days, and from 10 male and 10 female rats from all groups at 84 days of testing. Samples were analyzed for the following:

1. Hematologic Studies

- a. Total Leukocyte Count
- b. Erythrocyte Count
- c. Hemoglobin Concentration
- d. Hematocrit Value
- e. Cell Indices (MCV, MCH, MCHC)
- f. Differential Leukocyte Count
- g. Erythrocyte Morphology (Days 30 and 84 only)

2. Clinical Blood Chemistry Studies

- a. Serum Alkaline Phosphatase Activity (SAP)
- b. Serum Glutamic-Pyruvic Transaminase Activity (SGPT)
- c. Blood Urea Nitrogen Concentration (BUN)
- d. Fasting Blood Glucose Concentration
- e. Serum Glutamic-Oxalacetic Transaminase Activity (SGOT)

3. Urinalyses

- a. Glucose Concentration
- b. Albumin Concentration
- c. Microscopic Elements Examination
- d. pH
- e. Specific Gravity
- f. Aminolevulinic Acid Concentration (ALA Concentrations were determined at Days 0, 30, 60, and 84)

Statistical analyses were conducted on all hematologic and clinical blood chemistry data.

H. Blood Lead Determinations

Blood lead determinations were conducted on 20 male and 20 female control rats at 0-day, and on 10 male and 10 female rats from each group at 30, 60, and 84 days of testing.

I. Pathologic Studies

1. Gross Pathology

Following 90 days of feeding, all surviving rats were sacrificed by carbon dioxide asphyxiation and autopsied. Animals which died during the study were examined grossly and tissues preserved except in cases where advanced autolysis precluded meaningful evaluation. At autopsy, each animal received a complete gross examination and a complete set of organs and other tissues were removed and preserved in a formalin solution.

2. Organ Weights, Organ to Body Weight Ratios, and Organ to Brain Weight Ratios

The weights of the adrenals, brain, gonads, heart, kidneys, liver, spleen, and thyroid gland of each rat were recorded at the time of autopsy. Statistical analyses were conducted upon the absolute organ weights. An Analysis of Variance was conducted first and any significant effects disclosed were further analyzed by either the Tukey's (equal population size) or the Scheffe's (unequal population size) Multiple Comparison Test. Organ weight ratios to the body and brain were first analyzed by the Kruskal-Wallis Statistic test and any significant effects were further analyzed by the Kruskal-Wallis Multiple Comparison Test.

3. Tissue Analyses

Samples of tissues (liver, kidney, brain, and bone) were taken from 5 males and 5 females from each group at the time of autopsy and were analyzed for the lead and chromium content.

4. Microscopic Examination

Microscopic examination was conducted on tissues taken from 20 rats of each sex from the Control-I, Control-II, PC-III and T-III groups. Tissues, stained with Hematoxylin-Eosin, included the following: adrenals, urinary bladder, bone marrow, brain, colon, gonads, heart, kidneys, liver, lungs, cecum, eye, optic nerve, peripheral nerve, pituitary gland, mammary glands, small intestine (duodenum, ileum, and jejunum), spinal cord, uterus, lymph node (cervical and mesenteric), skeletal muscle, pancreas, parathyroid, prostate, spleen, stomach (cardia, fundus, and pylorus), and thyroid. Sections of kidney taken from 10 rats of each sex from the PC-I, PC-II, T-I, and T-II groups were also examined microscopically.

IV. Results

A. Body Weight

Body weight data collected during the 90-day test period are summarized in Table II. Also included in the table are 90-day average total weight gains. Body weights and body weight gains for the PC-III (20,000 ppm) and T-III (20,000 ppm) animals were noticeable lower and statistically different, in most cases, when compared to either Control-I or Control-II. The PC-III animals were more affected than the T-III animals. The weight gains for the PC-II (5,000 ppm) animals were also lower than the controls. In most cases, males showed lower body weight gains than females at these levels. The males and females from PC-I and T-I levels (both 2,000 ppm) and from the T-II level (5,000 ppm) compared favorably with the control groups.

TABLE II
TEST MATERIAL: Primrose Chrome Yellow
90-Day Subacute Oral Toxicity Study - Albino Rats
Body Weight and Total Weight Gain Data - Males
Summary of Mean Values

Group and Dietary Level (ppm)	0	1	2	3	4	5	6	7	8	9	10	11	12	13	Total Weight Gain (g/rat)
Control I (0)	129	204	242	271	287	322	347	374	381	402	419	428	443	442	313
Control II (0)	129	202	252	285	305	337	361	395	396	427	448	461	475	489	360
PC I (2,000)*	129	188	227	253	273	308	334	366	375	397	414	422	435	446	317
PC II (5,000)*	129	175 ^{bd}	211 ^{ad}	246 ^d	252	286	309 ^c	339 ^c	344 ^c	363 ^d	378 ^d	389 ^d	401 ^d	411 ^d	282
PC III (20,000)*	129	157 ^{bd}	190 ^{bd}	213 ^{bd}	237 ^d	262 ^{ad}	275 ^{bd}	301 ^{bd}	304 ^{bd}	323 ^{bd}	333 ^{bd}	345 ^{bd}	352 ^{bd}	367 ^{bd}	238
F I (2,000)	129	189	230	256	275	311	336	366	367	391	411	420	428	449	320
F II (5,000)	129	191	232	256	272	300	324	353	356	384	403	414	422	442	313
F III (20,000)	129	176 ^{bd}	212 ^{ad}	240 ^d	260	289	308 ^c	334 ^d	337 ^d	359 ^d	376 ^d	383 ^d	387 ^{ad}	397 ^d	266

* Statistically significant difference at the 95 percent confidence level from Control-I.

b Statistically significant difference at the 99 percent confidence level from Control-I.

c Statistically significant difference at the 95 percent confidence level from Control-II.

d Statistically significant difference at the 99 percent confidence level from Control-II.

* Lead Carbonate

TABLE II continued

TEST MATERIAL: Primrose Chrome Yellow

90-Day Subacute Oral Toxicity Study - Albino Rats

Body Weight and Total Weight Gain Data - Females

Summary of Mean Values

Group and Dietary Level (µgm)	Body Weight (g)													Total Weight Gain (g/rat)	
	0	1	2	3	4	5	6	7	8	9	10	11	12		13
Control I (0)	125	164	187	198	201	224	231	246	236	255	262	262	275	274	149
Control II (0)	125	159	183	199	208	225	235	244	246	251	257	261	270	269	144
PC I (2,000)*	125	155	175	187	193	215	225	239	229	252	259	261	270	264	139
PC II (5,000)*	125	148 ^b	165 ^{bd}	176 ^{bd}	182 ^c	204	217	229	220 ^d	236	241	245	254	253	128
PC III (20,000)*	125	141 ^{bd}	162 ^{bd}	172 ^{bd}	186	206	214	222 ^a	206 ^{bd}	229	232 ^a	237	243 ^a	243 ^a	118
T I (2,000)	125	157	177	191	200	224	230	242	247	251	261	264	272	272	147
T II (5,000)	125	160	178	195	201	222	232	243	246	252	259	261	269	269	144
T III (20,000)	125	146 ^{bd}	170 ^a	185	191	209	217	229	231	235	243	243	251	250	125

a Statistically significant difference at the 95 percent confidence level from Control-I.

b Statistically significant difference at the 99 percent confidence level from Control-I.

c Statistically significant difference at the 95 percent confidence level from Control-II.

d Statistically significant difference at the 99 percent confidence level from Control-II.

* Lead Carbonate

B. Food Consumption

Mean food consumption data collected during the 90-day test period are summarized in Table III. Total food intake for the PC-II (5,000 ppm), PC-III (20,000 ppm), and T-III (20,000 ppm) male animals was somewhat lower (-12%, -19%, and -10% respectively) than that of the control groups. Food intake for all positive control and T-III females was low only during the first 2 or 3 weeks of testing. The PC-I (2,000 ppm), T-I (2,000 ppm), and T-II (5,000 ppm) groups consumed amounts of food considered comparable to the control groups during the investigation.

TABLE III
TEST MATERIAL: Primrose Chrome Yellow
90-Day Subacute Oral Toxicity Study - Albino Rats

Food Consumption Data - Males

Summary of Mean Values

Group and Dietary Level (ppm)	Food Consumption (g/rat/7 days)													Total Food Consumption (g/rat)
	Week:													
	1	2	3	4	5	6	7	8	9	10	11	12	13	
Control-I (0)	111	148	167	168	174	183	177	188	184	183	179	174	163	2,199
Control-II (0)	101	153	174	181	148	156	161	179	167	166	178	200	184	2,148
PC-I (2,000)*	112	130	138	149	163	172	180	186	177	178	180	178	169	2,112
PC-II (5,000)*	102	136	132	141	136	148	145	162	162	159	164	159	165	1,911
PC-III (20,000)*	70	106	120	139	129	151	136	147	150	156	145	152	162	1,763
T-I (2,000)	120	153	157	152	154	169	169	169	164	166	180	179	191	2,123
T-II (5,000)	116	144	150	134	144	149	160	167	166	175	174	176	179	2,034
T-III (20,000)	114	131	131	151	148	158	152	159	159	157	157	164	168	1,949

* Lead Carbonate

TABLE III continued
 TEST MATERIAL: Primrose Chrome Yellow
 90-Day Subacute Oral Toxicity Study - Albino Rats

Food Consumption Data - Females

Summary of Mean Values

Group and Dietary Level (ppm)	Food Consumption (g/rat/7 days)													Total Food Consumption (g/rat)
	Week:													
	1	2	3	4	5	6	7	8	9	10	11	12	13	
Control-I (0)	101	131	121	114	99	113	117	124	120	117	125	112	118	1,512
Control-II (0)	91	125	131	129	123	130	127	130	117	117	118	128	109	1,575
PC-I (2,000)*	82	114	128	126	113	116	119	126	119	118	119	116	108	1,504
PC-II (5,000)*	76	100	114	117	100	107	116	132	112	111	110	112	111	1,418
PC-III (20,000)*	57	88	113	124	115	120	112	119	114	120	117	110	113	1,422
T-I (2,000)	94	125	129	136	126	140	140	133	123	127	129	125	128	1,655
T-II (5,000)	102	126	117	126	125	142	131	130	131	128	118	121	126	1,623
T-III (20,000)	96	104	111	118	117	121	127	114	136	115	123	119	118	1,519

* Lead Carbonate

C. Mortality and Reactions

A summary of the number of mortalities that occurred during the study is presented in Table IV. The mortalities that occurred during the study, with the exception of one 2,000 ppm female, were a result of trauma incurred at blood collection.

No untoward behavioral reactions were noted among any of the animals in the study.

TABLE IV

TEST MATERIAL: Primrose Chrome Yellow

90-Day Subacute Oral Toxicity Study - Albino Rats

Summary of Mortalities

Group and Dietary Level (ppm)	Sex	Animal Number	Days on Test	Probable Cause of Death
Control-I (0)	M	-	-	-
	F	38	30	Trauma at blood collection
Control-II (0)	M	-	-	-
	F	-	-	-
PC-I (2,000)*	M	-	-	-
	F	112	84	Trauma at blood collection
PC-II (5,000)*	M	-	-	-
	F	-	-	-
PC-III (20,000)*	M	171	30	Trauma at blood collection
	F	187	84	Trauma at blood collection
		189	30	Trauma at blood collection
		190	30	Trauma at blood collection
		191	30	Trauma at blood collection
		192	30	Trauma at blood collection
		193	30	Trauma at blood collection
		194	30	Trauma at blood collection
		195	30	Trauma at blood collection
		196	84	Trauma at blood collection
T-I (2,000)	M	-	-	-
	F	474	35	Unknown
		478	84	Trauma at blood collection
T-II (5,000)	M	-	-	-
	F	-	-	-
T-III (20,000)	M	536	30	Trauma at blood collection
	F	546	84	Trauma at blood collection
		548	84	Trauma at blood collection
		552	30	Trauma at blood collection

- = No animals succumbed.

* Lead Carbonate

D. Hematologic Studies

The results of the hematologic studies conducted are presented in Tables V through VII.

The positive control groups fed 5,000 ppm (PC-II) or 20,000 ppm (PC-III) of lead carbonate exhibited statistically significant reductions in the hemoglobin concentrations and hematocrit values after 30 days (PC-III only) and 84 days of testing. The mean corpuscular volume, mean corpuscular hemoglobin, and mean corpuscular hemoglobin concentration were reduced for the PC-II females (not males), in most cases, at 84 days and for the PC-III animals at 30 and 84 days. Positive control animals fed 2,000 ppm (PC-I) exhibited either normal hematologic values or values which were comparable to those of the controls during the investigation. The PC-III animals exhibited slight increases in erythrocyte counts after 84 days of testing. The lower PC-I and PC-II groups exhibited erythrocyte counts that were comparable to those of the controls.

The hemoglobin concentration and hematocrit value of the T-II (5,000 ppm) males (not females) at 84 days and of the T-III (20,000 ppm) males and females at 30 and 84 days was significantly reduced when compared to either control group. The mean corpuscular volume, mean corpuscular hemoglobin and the mean corpuscular hemoglobin concentration of males and females fed 5,000 ppm or 2,000 ppm of Primrose Chrome Yellow were slightly to moderate reduced, in most cases, at 30 days (T-III) and 84 days (T-II and T-III). The T-I (2,000 ppm) animals exhibited values comparable to the controls for all of the above hematologic studies. The erythrocyte counts of the T-I, T-II, and T-III males and females were comparable to the control animals.

Slight to marked variations were noted in the size, shape, or color (PC-III only) of the erythrocytes in most males from the PC-III, T-I, T-II, and T-III groups after 84 days of testing. The color of erythrocytes from all test males (T-I through T-III) appeared normal during the investigation. The PC-I and PC-II males exhibited normal erythrocyte morphology. Slight to moderate variations in erythrocyte morphology were noted for all females fed lead carbonate and only females fed 20,000 ppm (T-III) of Primrose Chrome Yellow after 84 days of testing. The females fed 2,000 ppm (T-I) or 5,000 ppm (T-II) of Primrose Chrome Yellow exhibited normal erythrocyte morphology.

The total leukocyte counts and differential leukocyte counts for animals fed either lead carbonate or Primrose Chrome Yellow were considered normal for albino rats of this age and strain in this laboratory.

TABLE V

TEST MATERIAL: Primrose Chrome Yellow
90 Day Subacute Oral Toxicity Study - Albino Rats

Hematologic Data - Males

Summary of Mean Values

Group and Dietary Level (ppm)	Total Leukocyte Count (thousands/mm ³)			Erythrocyte Count (millions/mm ³)			Hemoglobin Concentration (g/100 ml)			Hematocrit Value (percent)		
	0	30	84	0	30	84	0	30	84	0	30	84
Control I (0)	9.1	9.8	10.4	6.10	8.00	8.52	13.1	16.4	16.5	36.4	42.9	41.4
Control II (0)	5.5	11.3	9.3	6.11	7.72	8.70	13.2	15.8	16.5	36.4	41.0	44.2
PC I (2,000)*	-	-	9.7	-	-	8.30	-	-	15.6	-	-	38.5
PC II (5,000)*	-	-	12.6	-	-	8.65	-	-	14.8 ^{bd}	-	-	37.4 ^d
PC III (20,000)*	-	12.2	12.3	-	7.89	9.16 ^b	-	12.7 ^{bd}	12.7 ^{bd}	-	34.9 ^{bd}	34.6 ^{bd}
T I (2,000)	-	-	9.6	-	-	8.69	-	-	15.7	-	-	40.9
T II (5,000)	-	-	9.6	-	-	8.67	-	-	14.8 ^{bd}	-	-	37.9 ^d
T III (20,000)	-	11.6	12.8	-	7.72	8.61 ^b	-	12.7 ^{bd}	10.9 ^{bd}	-	34.5 ^{bd}	29.5 ^{bd}

^b Statistically significant difference at the 99 percent confidence level from Control-I.

^d Statistically significant difference at the 99 percent confidence level from Control-II.

- Analysis not conducted

* Lead Carbonate

TABLE V continued

TEST MATERIAL: Primrose Chrome Yellow
90-Day Subacute Oral Toxicity Study - Albino Rats

Hematologic Data - Females

Summary of Mean Values

Group and Dietary Level (ppm)	Total Leukocyte Count (thousands/mm ³)			Erythrocyte Count (millions/mm ³)			Hemoglobin Concentration (g/100 ml)			Hematocrit Value (percent)		
	Day: 0	30	84	Day: 0	30	84	Day: 0	30	84	Day: 0	30	84
Control I (0)	7.1	9.3	7.7	6.39	7.50	7.77	13.6	15.4	15.7	36.2	39.3	38.7
Control II (0)	7.5	8.1	7.8	6.33	7.42	7.93	13.6	15.2	15.6	36.3	38.1	39.0
PC I (2,000)*	-	-	7.5	-	-	7.84	-	-	15.4	-	-	37.7
PC II (5,000)*	-	-	7.0	-	-	7.85	-	-	14.5	-	-	35.5 ^{ac}
PC III (20,000)*	-	11.5	9.1	-	7.78	8.45 ^a	-	13.1 ^{bd}	13.1 ^{bd}	-	34.9 ^{bd}	34.0 ^{bd}
T I (2,000)	-	-	3.3	-	-	7.94	-	-	15.2	-	-	37.8
T II (5,000)	-	-	9.4	-	-	8.08	-	-	14.6	-	-	36.4
T III (20,000)	-	12.4 ^d	8.0	-	6.88 ^a	7.89	-	12.7 ^{bd}	10.8 ^{bd}	-	31.2 ^{bd}	28.7 ^{bd}

^a Statistically significant difference at the 95 percent confidence level from Control I.

^b Statistically significant difference at the 99 percent confidence level from Control I.

^c Statistically significant difference at the 95 percent confidence level from Control-II.

^d Statistically significant difference at the 99 percent confidence level from Control-II.

- Analysis not conducted

* Lead Carbonate

TABLE V continued
TEST MATERIAL: Primrose Chrome Yellow

90-Day Subacute Oral Toxicity Study - Albino Rats

Hematologic Data - Males

Summary of Mean Values

Group and Dietary Level (ppm)	Mean Corpuscular Volume (μ^3)			Mean Corpuscular Hemoglobin (μg)			Mean Corpuscular Hemoglobin Concentration (percent)		
	0	30	84	0	30	84	0	30	84
Control I (0)	60.2	54.1	49.5	21.6	20.6	19.5	36.0	38.2	39.8
Control II (0)	60.1	53.7	51.9	21.8	20.7	19.1	36.5	38.6	37.8
PC I (2,000)*	-	-	47.2 ^c	-	-	19.0	-	-	40.6
PC II (5,000)*	-	-	44.0 ^{bd}	-	-	17.3 ^{bd}	-	-	39.7
PC III (20,000)*	-	44.7 ^{bd}	38.5 ^{bd}	-	16.4 ^{bd}	14.2 ^{bd}	-	36.7 ^{bd}	37.0
F I (2,000)	-	-	48.0	-	-	18.2	-	-	38.5
F II (5,000)	-	-	44.5 ^{ad}	-	-	17.2 ^{bd}	-	-	39.1
F III (20,000)	-	45.0 ^{bd}	34.7 ^{bd}	-	16.7 ^{bd}	12.9 ^{bd}	-	36.9 ^{bd}	34.7 ^a

a. Statistically significant difference at the 95 percent confidence level from Control-I.

b. Statistically significant difference at the 99 percent confidence level from Control-I.

c. Statistically significant difference at the 95 percent confidence level from Control-II.

d. Statistically significant difference at the 99 percent confidence level from Control-II.

* Analytically not conducted

^a Lead Carbonate

TABLE V continued
TEST MATERIAL: Primrose Chrome Yellow
90-Day Subacute Oral Toxicity Study - Albino Rats

Hematologic Data - Females

Summary of Mean Values

Group and Dietary Level (ppm)	Mean Corpuscular Volume (μ^3)			Mean Corpuscular Hemoglobin (μg)			Mean Corpuscular Hemoglobin Concentration (percent)		
	0	30	84	0	30	84	0	30	84
Control I (0)	57.2	52.7	50.	21.5	20.5	20.4	37.6	39.3	40.7
Control II (0)	57.9	51.6	49.8	21.7	20.6	19.9	37.7	40.2	40.2
PC-I (2,000)*	-	-	48.8	-	-	19.7	-	-	40.9
PC-II (5,000)*	-	-	45.8 ^{bd}	-	-	18.7 ^b	-	-	41.1
PC-III (20,000)*	-	45.2 ^{bd}	41.0 ^{bd}	-	17.0 ^{bd}	15.7 ^{bd}	-	37.8 ^{ad}	38.7 ^{bd}
F-I (2,000)	-	-	48.3	-	-	19.3	-	-	40.4
F-II (5,000)	-	-	45.7 ^{bd}	-	-	18.2 ^{bd}	-	-	40.2
F-III (20,000)	-	45.4 ^{bd}	36.5 ^{bd}	-	18.5 ^{bd}	14.0 ^{bd}	-	41.0	38.2 ^{bd}

* Statistically significant difference at the 95 percent confidence level from Control-I.

b Statistically significant difference at the 99 percent confidence level from Control-I.

d Statistically significant difference at the 99 percent confidence level from Control-II.

- - Analysts not conducted

* Lead Carbonate

TABLE VI
TEST MATERIAL: Primrose Chrome Yellow
90 Day Subacute Oral Toxicity Study - Albino Rats

Hematologic Data - Males

Summary of Mean Values

Group and Dietary Level (ppm)	Differential Leukocyte Count (Number of Cells per Hundred)											
	Lymphocytes			Neutrophils			Monocytes			Eosinophils		
	Day:	30	84	Day:	30	84	Day:	30	84	Day:	30	84
Control I (0)	89	80	82	10	16	16	1	4	1	0	0	1
Control II (0)	89	86	84	10	12	12	1	2	4	0	0	0
PC I (2,000) ^a	-	-	84	-	-	15	-	-	1	-	-	0
PC II (5,000) ^a	-	-	81	-	-	17	-	-	1	-	-	1
PC III (20,000) ^a	-	87 ^a	82	-	10 ^a	16	-	3	2	-	0	0
T I (2,000)	-	-	84	-	-	12	-	-	3	-	-	1
T II (5,000)	-	-	81	-	-	13	-	-	6	-	-	0
T III (20,000)	-	84	81	-	14	13	-	2	6	-	0	0

^a Statistically significant difference at the 95 percent confidence level from Control-I.

^b Analysis not conducted

^c Lead Carbonate

TABLE VI continued
 TEST MATERIAL: Primrose Chrome Yellow
 90-Day Subacute Oral Toxicity Study - Albino Rats
 Hematologic Data - Females
 Summary of Mean Values

Group and Dietary Level (ppm)	Lymphocytes			Neutrophils			Monocytes			Eosinophils			Basophils		
	Day:	30	84	Day:	30	84	Day:	30	84	Day:	30	84	Day:	30	84
Control I (0)	93	82	81	7	15	16	0	3	2	0	0	1	0	0	0
Control II (0)	92	83	82	7	14	15	1	3	2	0	0	1	0	0	0
PC I (2,000) *	-	-	84	-	-	14	-	-	1	-	-	1	-	-	0
PC II (5,000) *	-	-	83	-	-	16	-	-	0	-	-	1	-	-	0
PC-III (20,000) *	-	83	84	-	14	16	-	2	0	-	1	0	-	0	0
T-I (2,000)	-	-	82	-	-	15	-	-	2	-	-	1	-	-	0
T-II (5,000)	-	-	86	-	-	12	-	-	1	-	-	1	-	-	0
T-III (20,000)	-	90 ^a	85	-	8 ^a	14	-	2	1	-	0	0	-	0	0

^a Statistically significant difference at the 95 percent confidence level from Control-I.

- = Analysis not conducted

* Lead Carbonate

TABLE VII
TEST MATERIAL: Primrose Chrome Yellow
90-Day Subacute Oral Toxicity Study - Albino Rats

Hematologic Data - Males
Summary of Mean Values

Group and Dietary Level (ppm)	Size ^a			Erythrocyte Morphology Shape ^b			Color ^c	
	30	84	Day:	30	84	Day:	30	84
Control-I (0)	n	n		n	n		n	n
Control-II (0)	n	n		n	n		n	n
PC-I (2,000)*	-	n		-	n		-	n
PC-II (5,000)*	-	n		-	n		-	n
PC-III (20,000)*	n	+(a)		n	++		n	+(a), +(b)
T-I (2,000)	-	+(a)		-	+		-	n
T-II (5,000)	-	+(a)		-	+		-	n
T-III (20,000)	n	+++ (a)		n	+++		n	n

Key: ^a (a) Anisocytosis (variation in cell size)

(b) Macrocytosis (larger than normal)

(c) Microcytosis (smaller than normal)

(d) Poikilocytosis (variation in cell shape)

^c (a) Hypochromia (less than normal cell color)

(b) Polychromasia (cells do not stain evenly)

Grade: n = normal

+ = slight

++ = moderate

+++ = marked

* Lead Carbonate

TABLE VII continued
 TEST MATERIAL: Primrose Chrome Yellow
 90-Day Subacute Oral Toxicity Study - Albino Rats

Hematologic Data - Females
 Summary of Mean Values

Group and Dietary Level (ppm)	Size ^a			Erythrocyte Morphology Shape ^b			Color ^c	
	30	84	Day:	30	84	Day:	30	84
Control I (0)	n	n		n	+		n	n
Control II (0)	n	n		n	n		n	n
PC I (2,000)*	-	n		-	+		-	+(b)
PC II (5,000)*	-	+(a)		-	+		-	+(b)
PC III (20,000)*	n	++(a)		n	++		n	++(b)
T I (2,000)	-	n		-	n		-	n
T II (5,000)	-	n		-	+		-	n
T III (20,000)	n	-(b), +(c)		n	+		n	+(a), +(b)

Key:
 (a) Anisocytosis (variation in cell size)
 (b) Macrocytosis (larger than normal)
 (c) Microcytosis (smaller than normal)
 + Microcytosis (variation in cell shape)
 * (a) Hypochromia (less than normal cell color)
 (b) Polychromasia (cells do not stain evenly)

Grade:
 n = normal
 + = slight
 ++ = moderate
 +++ = marked
 * Lead Carbonate

E. Clinical Blood Chemistry Studies

The results of the clinical chemistry studies conducted at 0, 30, and 84 days of testing are summarized in Table VIII. Slight increases in serum alkaline phosphatase (SAP) activity were exhibited by animals fed 5,000 ppm (PC-II) or 20,000 ppm (PC-III) of lead carbonate after 84 days of testing. However, the SAP activity of the PC-II and PC-III animals was within the normal range. The animals fed 2,000 ppm (PC-I) of lead carbonate exhibited SAP activity which was comparable to that of the controls. Slight elevations in SAP activity were noted in animals fed 20,000 ppm Primrose Chrome Yellow after 84 days of testing. The T-I and T-II animals exhibited SAP activity comparable to that of the controls.

Serum glutamic-pyruvic transaminase (SGPT) activity was slightly reduced in the females (not males) fed 5,000 ppm (PC-II) or 20,000 ppm (PC-III) of lead carbonate after 84 days of testing. All other positive control groups and all test groups exhibited SGPT activity comparable to that of the control animals.

Serum glutamic-oxalacetic transaminase activity (SGOT) was moderately elevated for the PC-III (20,000 ppm) females (not males) after 30 days of feeding lead carbonate. Normal SGOT activity was exhibited by all positive control groups (PC-I through PC-III) after 84 days. The males and females from all groups (T-I through T-III) fed Primrose Chrome Yellow exhibited SGOT activity comparable to the controls during the investigation.

The results of the remaining clinical blood chemistry studies, fasting blood glucose concentration and blood urea nitrogen concentration, were considered normal for albino rats of this age and strain fed either lead carbonate or Primrose Chrome Yellow.

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TABLE VIII

TEST MATERIAL: Primrose Chrome Yellow

90-Day Subacute Oral Toxicity Study - Albino Rats

Clinical Blood Chemistry Data - Males

Summary of Mean Values

Group and Dietary Level	Serum Alkaline Phosphatase			Serum Glutamic Pyruvic Transaminase Activity			Blood Urea Nitrogen			Fasting Blood Glucose			Serum Glutamic-Oxalacetic Transaminase Activity		
	(International Units/L)			(International Units/L)			(mg/100 ml)			(mg/100 ml)			(International Units/L)		
	Day: 0	30	84	Day: 0	30	84	Day: 0	30	84	Day: 0	30	84	Day: 0	30	84
Control I (0)	118	84	56	34	29	30	16	12	12	104	123	116	100	62	68
Control II (0)	129	98	66	4	32	32	19	12	15	114	127	141	106	62	75
PC I (2,000)*	-	-	64	-	-	31	-	-	11 ^d	-	-	115 ^d	-	-	77
PC II (5,000)*	-	-	71	-	-	29	-	-	12	-	-	115 ^d	-	-	70
PC III (20,000)*	100	76 ^a	-	21	27	-	15	13	-	128	121 ^c	-	64	77	-
T I (2,000)	-	-	74	-	-	33	-	-	13	-	-	140	-	-	74
T II (5,000)	-	-	72	-	-	31	-	-	13	-	-	141	-	-	73
T III (20,000)	94	90 ^d	-	20 ^c	27	-	12	11 ^d	-	121	131	-	-	66	76

* Statistically significant difference at the 95 percent confidence level from Control-I.

c Statistically significant difference at the 95 percent confidence level from Control-II.

d Statistically significant difference at the 99 percent confidence level from Control-II.

- Analysis not conducted.

* Lead Carbonate

TABLE VIII continued

TEST MATERIAL: Primrose Chrome Yellow

90-Day Subacute Oral Toxicity Study - Albino Rats

Clinical Blood Chemistry Data - Females

Summary of Mean Values

Group and Dosing Level (ppm)	Serum Alkaline Phosphatase Activity (International Units/L)			Serum Glutamic-Pyruvic Transaminase Activity (International Units/L)			Blood Urea Nitrogen Concentration (mg/100 ml)			Fasting Blood Glucose Concentration (mg/100 ml)			Serum Glutamic-Oxalacetic Transaminase Activity (International Units/L)		
	0	30	84	0	30	84	0	30	84	0	30	84	0	30	84
Control I (0)	93	50	27	26	28	38	17	14	14	117	129	122	94	66	72
Control II (0)	112	55	34	27	18	33	17	13	15	115	122	128	89	53	60
PC-I (2,000)*	-	-	33	-	-	27	-	-	12 ^c	-	-	122	-	-	63
PC-II (5,000)*	-	-	44	-	-	21	-	-	12	-	-	126	-	-	60
PC-III (20,000)*	-	52	42	-	21	21	-	13	14 ^d	-	121	143	-	95 ^d	70
T-I (2,000)	-	-	38	-	-	25	-	-	14	-	-	127	-	-	55
T-II (5,000)	-	-	43	-	-	23	-	-	14	-	-	128	-	-	59
T-III (20,000)	-	58	61 ^d	-	19	26	-	12	14	-	120	130	-	84	72

* Statistically significant difference at the 95 percent confidence level from Control-II.

d Statistically significant difference at the 99 percent confidence level from Control-II.

- Analysis not conducted.

* Lead Carbonate

F. Urinalyses

The results of the urinalyses conducted at 0, 30 and 84 days are presented in Table IX. The results of the determinations for Aminolevulinic Acid (ALA) concentration conducted at 0, 30, 60 and 84 days are presented in Table X. The routine urinalyses showed no noticeable differences for the values of positive control or test animals when compared to those of the control animals.

Noticeable increases were observed in the ALA concentrations of both the PC-III (20,000 ppm) and T-III (20,000 ppm) animals when compared to the controls after 30 days of testing. Statistically significant differences were observed in the PC-II (5,000 ppm) and T-II (5,000 ppm) groups and in the PC-III (20,000 ppm) and T-III (20,000 ppm) groups when compared to either Control-I or Control-II. Statistically differences were noted for the PC-I (2,000 ppm) males, when compared to the controls, only at the 60-day examination. The ALA concentrations of animals fed lead carbonate were greater than those of the animals fed Primrose Chrome Yellow at the same dietary levels.

TABLE IX

TEST MATERIAL: Primrose Chrome Yellow
90-Day Subacute Oral Toxicity Study - Albino Rats

Urinalyses Data - Males

Summary of Mean Values

Group and Dietary Level (ppm)	Glucose			Albumin			Microscopic Elements**			pH			Specific Gravity		
	0	30	84	0	30	84	0	30	84	0	30	84	0	30	84
Control-I (0)	n	n	n	n	t	t	t	t	n	6.9	6.8	7.0	1.021	1.025	1.023
Control-II (0)	n	n	n	n	n	t	+1	t	t	6.9	6.8	6.8	1.022	1.020	1.023
PC-III (20,000) *	-	n	n	-	t	t	-	n	n	-	6.9	7.0	-	1.018	1.015
T-III (20,000)	-	n	n	-	t	t	-	n	n	-	6.2	6.6	-	1.020	1.022

Key: n = negative or normal
t = minimal or trace
+1 = slight amounts
+2 = moderate amounts
+3 = large amounts

- = Analysis not conducted.

* Lead Carbonate

** Crystals

TABLE IX continued
 TEST MATERIAL: Primrose Chrome Yellow
 90-Day Subacute Oral Toxicity Study - Albino Rats

Urinalyses Data - Females

Summary of Mean Values

Group and Dietary Level (ppm)	Glucose		Albumin		Microscopic Elements**		pH		Specific Gravity	
	Day: 0	Day: 30	Day: 0	Day: 30	Day: 0	Day: 30	Day: 0	Day: 30	Day: 0	Day: 30
Control-I (0)	n	n	n	n	+1	n	6.9	6.4	1.018	1.015
Control-II (0)	n	n	n	n	+2	n	6.8	6.5	1.022	1.015
PC-III (20,000)*	-	n	-	n	-	n	-	7.0	-	1.012
T-III (20,000)	-	n	-	n	-	n	-	6.5	-	1.010

Key: n = negative or normal
 + = minimal or trace
 +1 = slight amounts
 +2 = moderate amounts
 +3 = large amounts

- = Analysis not conducted.

* Lead Carbonate

** Crystals

TABLE X

TEST MATERIAL: Primrose Chrome Yellow
90-Day Subacute Oral Toxicity Study - Albino Rats

Urinalyses Data - Males

Summary of Mean Values

Group and Dietary Level (ppm)	Aminolevulinic Acid Concentration (ALA) (mg/100 ml)			
	Day:			
	0	30	60	84
Control-I (0)	0.31	0.57	0.47	0.33
Control-II (0)	-	0.44	0.40	0.34
PC-I (2,000)*	-	-	3.12 ^{bd}	1.61
PC-II (5,000)*	-	-	4.42 ^{bd}	2.66 ^{bd}
PC-III (20,000)*	-	4.36 ^{bd}	5.36 ^{bd}	5.43 ^{bd}
T-I (2,000)	-	-	1.02 ^f	0.84
T-II (5,000)	-	-	1.94 ^h	2.01 ^{ac}
T-III (20,000)	-	3.50 ^{bd}	4.54 ^{bd}	5.39 ^{bd}

- a Statistically significant difference at the 95 percent confidence level from Control-I.
b Statistically significant difference at the 99 percent confidence level from Control-I.
c Statistically significant difference at the 95 percent confidence level from Control-II.
d Statistically significant difference at the 99 percent confidence level from Control-II.
f Statistically significant difference at the 99 percent confidence level from PC-I.
h Statistically significant difference at the 99 percent confidence level from PC-II.

- = Analysis not conducted.

* Lead Carbonate

TABLE X continued

TEST MATERIAL: Primrose Chrome Yellow
90-Day Subacute Oral Toxicity Study - Albino Rats

Urinalyses Data - Females

Summary of Mean Values

Group and Dietary Level (ppm)	Aminolevulinic Acid Concentration (ALA) (mg/100 ml)			
	Day:			
	0	30	60	84
Control-I (0)	0.28	0.27	0.37	0.47
Control-II (0)	-	0.34	0.36	0.66
PC-I (2,000)*	-	-	1.15	1.68
PC-II (5,000)*	-	-	2.61 ^{bd}	3.67 ^{bd}
PC-III (20,000)*	-	3.68 ^{bd}	3.99 ^{bd}	5.45 ^{bd}
T-I (2,000)	-	-	0.74	1.25
T-II (5,000)	-	-	2.27 ^{ac}	2.66 ^{ac}
T-III (20,000)	-	2.38 ^{bdj}	4.43 ^{bd}	4.68 ^{bd}

- a Statistically significant difference at the 95 percent confidence level from Control-I.
b Statistically significant difference at the 99 percent confidence level from Control-I.
c Statistically significant difference at the 95 percent confidence level from Control-II.
d Statistically significant difference at the 99 percent confidence level from Control-II.
j Statistically significant difference at the 99 percent confidence level from PC-III.

- = Analysis not conducted.

* Lead Carbonate

G. Blood Lead Determinations

The results of blood lead determinations conducted at 0, 30, 60, and 84 days are presented in Table XI. Noticeable increases were observed in the blood lead concentrations of all positive controls and test animals after 30, 60, and 84 days of testing. The increases in blood lead concentrations were dose-related. The blood lead concentrations of the animals fed lead carbonate were greater than those of the animals fed Primrose Chrome Yellow at the same dietary level.

TABLE XI

TEST MATERIAL: Primrose Chrome Yellow
 90-Day Subacute Oral Toxicity Study - Albino Rats
 Blood Lead Determinations - Males

Summary of Mean Values

Group and Dietary Level (ppm)	Blood Lead Concentration ($\mu\text{g}/100\text{ ml}$)			
	Day:			
	0	30	60	84
Control-I (0)	11	15	12	10
Control-II (0)	18	18	11	12
PC-I (2,000)*	-	61 ^{b,d}	70 ^{b,d}	70 ^{b,d}
PC-II (5,000)*	-	112 ^{b,d}	133 ^{b,d}	122 ^{b,d}
PC-III (20,000)*	-	213 ^{b,d}	271 ^{b,d}	280 ^{b,d}
T-I (2,000)	-	50 ^{b,d}	59 ^{a,c}	53 ^{b,d}
T-II (5,000)	-	65 ^{b,d,h}	80 ^{b,d,h}	82 ^{b,d,g}
T-III (20,000)	-	106 ^{b,d,j}	176 ^{b,d,j}	148 ^{b,d,j}

Note: Stock ration assayed at 0.55 ± 0.04 ppm of lead.

- = Analysis not conducted.

* Lead Carbonate

- a Statistically significant difference at the 95 percent confidence level from Control-I.
- b Statistically significant difference at the 99 percent confidence level from Control-I.
- c Statistically significant difference at the 95 percent confidence level from Control-II.
- d Statistically significant difference at the 99 percent confidence level from Control-II.
- e Statistically significant difference at the 95 percent confidence level from PC-II.
- h Statistically significant difference at the 99 percent confidence level from PC-II.
- j Statistically significant difference at the 99 percent confidence level from PC-III.

TABLE XI continued

TEST MATERIAL: Primrose Chrome Yellow
90-Day Subacute Oral Toxicity Study - Albino Rats

Blood Lead Determinations - Females

Summary of Mean Values

Group and Dietary Level (ppm)	Blood Lead Concentration ($\mu\text{g}/100\text{ ml}$)			
	Day:			
	0	30	60	84
Control-I (0)	13	14	9	13
Control-II (0)	14	14	7	11
PC-I (2,000)*	-	62 ^{b,d}	78 ^{b,d}	75 ^{b,d}
PC-II (5,000)*	-	91 ^{b,d}	116 ^{b,d}	99 ^{b,d}
PC-III (20,000)*	-	200 ^{b,d}	208 ^{b,d}	208 ^{b,d}
T-I (2,000)	-	42 ^{b,c}	50 ^{b,d,e}	49 ^{b,d}
T-II (5,000)	-	69 ^{b,d}	78 ^{b,d,h}	71 ^{b,d,g}
T-III (20,000)	-	133 ^{b,d,j}	149 ^{b,d,j}	128 ^{b,d,j}

Note: Stock ration assayed at 0.55 ± 0.04 ppm of lead.

- = Analysis not conducted.

* Lead Carbonate

- ^b Statistically significant difference at the 99 percent confidence level from Control-I.
- ^c Statistically significant difference at the 95 percent confidence level from Control-II.
- ^d Statistically significant difference at the 99 percent confidence level from Control-II.
- ^e Statistically significant difference at the 95 percent confidence level from PC-I.
- ^g Statistically significant difference at the 95 percent confidence level from PC-II.
- ^h Statistically significant difference at the 99 percent confidence level from PC-II.
- ^j Statistically significant difference at the 99 percent confidence level from PC-III.

H. Pathologic Studies

1. Gross Pathologic Findings

The findings noted upon gross pathologic examination were similar for control, positive control, and test animals.

2. Organ Weight and Organ to Body Weight and Organ to Brain Weight Ratio Data

The results of the statistical analyses conducted on absolute organ weights, organ to body weight and organ to brain weight ratios are summarized in Tables XII through XIX. Slight increases in kidney weights and ratios were observed in all of the positive control groups fed lead carbonate (PC-I, PC-II, and PC-III). The females fed 5,000 ppm (PC-II) and the males and females fed 20,000 ppm (PC-III) of lead carbonate exhibited increased spleen weights and ratios. The animals fed 5,000 ppm (T-II) or 20,000 ppm (T-III) Primrose Chrome Yellow exhibited slight increases in kidney weight and kidney to body weight ratios. No differences in kidney weights and ratios were noted between the control animals and the animals fed 2,000 ppm (T-I) Primrose Chrome Yellow. Other statistically significant differences noted either were considered normal for a random population of albino rats of this age and strain or were attributed to body weight reductions observed in some of the groups (the groups fed 5,000 or 20,000 ppm of lead carbonate and the group fed 20,000 ppm of Primrose Chrome Yellow).

TABLE XII
TEST MATERIAL - PRIMROSE CHROME YELLOW
90-DAY SUBCUTANEOUS ORAL TOXICITY STUDY - ALBINO RATS

FINAL SACRIFICE

ORGAN WEIGHT AND RATIO DATA

SUMMARY OF MEAN VALUES

ORGAN - ADRENAL GLANDS

GROUP	TREATMENT (PPM)	ORGAN WEIGHT (GM)		ORGAN/BODY WEIGHT RATIO (GM/100 GM)		ORGAN/MAIN WEIGHT RATIO (GM/GM)	
		MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
CONTROL-I	0	0.063	0.071	0.0147	0.0256	0.0348	0.0426
CONTROL-II	0	0.057	0.068	0.0117	0.0249	0.0302	0.0380
PC-I	2,000*	0.063	0.068	0.0139	0.0250	0.0347	0.0404
PC-II	5,000*	0.058	0.064	0.0138	0.0248	0.0315	0.0375
PC-III	20,000*	0.053	0.071	0.0146	0.0284	0.0300	0.0416
T-I	2,000	0.059	0.068	0.0130	0.0241	0.0318	0.0384
T-II	5,000	0.050	0.071	0.0125	0.0257	0.0303	0.0407
T-III	20,000	0.053	0.067	0.0131	0.0255	0.0292	0.0396

NO STATISTICALLY SIGNIFICANT DIFFERENCES WERE NOTED.

* LEAD CARBONATE

TABLE XIII
TEST MATERIAL - PRIMROSE CHROME YELLOW
90-DAY SUBACUTE ORAL TOXICITY STUDY - ALBINO RATS

FINAL SACRIFICE

ORGAN WEIGHT AND RATIO DATA

SUMMARY OF MEAN VALUES

ORGAN - BRAIN

GROUP	DIETARY LEVEL (PPM)	ORGAN WEIGHT (GM)		ORGAN/BODY WEIGHT RATIO (GM/100 GM)		ORGAN/BRAIN WEIGHT RATIO (GM/GM)	
		MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
CONTROL-I	0	1.810	1.674	0.4164	0.6051	1.0000	1.0000
CONTROL-II	0	1.890	1.784	0.3888	0.6570	1.0000	1.0000
PC-I	2,000*	1.804	1.696	0.4021	0.6250	1.0000	1.0000
PC-II	5,000*	1.795	1.721	0.4395 ^c	0.6682	1.0000	1.0000
PC-III	20,000*	1.774	1.697	0.4871 ^{bd}	0.6852	1.0000	1.0000
T-I	2,000	1.855	1.770	0.4087	0.6286	1.0000	1.0000
T-II	5,000	1.854	1.742	0.4161	0.6343	1.0000	1.0000
T-III	20,000	1.813	1.692	0.4553 ^c	0.6510	1.0000	1.0000

b STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 99 PERCENT CONFIDENCE LEVEL FROM CONTROL-I.

c STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

d STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 99 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

* LEAD CARBONATE

TABLE XIV
TEST MATERIAL - PRIMROSE CHROME YELLOW
90-DAY SUBCUTANEOUS ORAL TOXICITY STUDY - ALBINO RATS

FINAL SACRIFICE

ORGAN WEIGHT AND RATIO DATA

SUMMARY OF MEAN VALUES

ORGAN - GONADS

GROUP	DIETARY LEVEL (PERCENT)	ORGAN WEIGHT (GM)		ORGAN/BODY WEIGHT RATIO (GM/100 GM)		ORGAN/BRAIN WEIGHT RATIO (GM/GM)	
		MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
CONTROL-I	0	3.189	0.082	0.7329	0.0293	1.7639	0.0488
CONTROL-II	0	3.283	0.085	0.6768	0.0312	1.7435	0.0477
PC-I	2,000*	3.552	0.089	0.7496	0.0326	1.9684 ^c	0.0528
PC-II	5,000*	3.386	0.079	0.8302 ^c	0.0304	1.8853	0.0458
PC-III	20,000*	3.281	0.079	0.9026 ^{ad}	0.0314	1.8545	0.0466
T-I	2,000	3.154	0.087	0.6994	0.0307	1.7097	0.0491
T-II	5,000	3.243	0.083	0.7253	0.0302	1.7557	0.0479
T-III	20,000	3.257	0.082	0.8170	0.0314	1.8027	0.0487

* STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-I.

^c STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

^d STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 99 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

* LEAD CARBONATE

TABLE XV
TEST MATERIAL - PHIMROSE CHROME YELLOW
90-DAY SUBACUTE ORAL TOXICITY STUDY - ALBINO RATS
FIPAL SACRIFICE

ORGAN WEIGHT AND RATIO DATA

SUMMARY OF MEAN VALUES

ORGAN - HEART

GROUP	DOSE (PPM)	ORGAN WEIGHT (G)		ORGAN/BODY WEIGHT RATIO (GM/100 GM)		ORGAN/BRAIN WEIGHT RATIO (GM/GM)	
		MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
CONTROL-I	0	1.559	1.085	0.3567	0.3897	0.8604	0.6485
CONTROL-II	0	1.631	1.017	0.3332	0.3744	0.8635	0.5705
PC-I	2,000*	1.521	1.056	0.3377	0.3875	0.8423	0.6249
PC-II	5,000*	1.430 ^c	1.038	0.3498	0.4014	0.8006	0.6027
PC-III	20,000*	1.343 ^{ad}	0.967	0.3667 ^c	0.3893	0.7577 ^a	0.5710
T-I	2,000	1.531	1.075	0.3376	0.3808	0.8284	0.6094
T-II	5,000	1.554	1.039	0.3477	0.3769	0.8406	0.5983
T-III	20,000	1.546 ^c	1.069	0.3868 ^c	0.4113	0.8565	0.6349

^a STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-I.

^c STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

^d STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 99 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

* LEAD CARBONATE

TABLE XVI

TEST MATERIAL - PRIMROSE CHROME YELLOW
90-DAY SUBCUTANEOUS ORAL TOXICITY STUDY - ALBINO RATS

FINAL SACRIFICE

ORGAN WEIGHT AND RATIO DATA

SUMMARY OF MEAN VALUES

ORGAN - KIDNEYS

GROUP	DIETARY LEVEL (PPM)	ORGAN WEIGHT (G)	ORGAN/BODY WEIGHT RATIO (GM/100 GM)		ORGAN/HAIR WEIGHT RATIO (GM/GM)	
			MALES	FEMALES	MALES	FEMALES
CONTROL-I	0	3.309	2.186	0.7730	0.7854	1.8622
CONTROL-II	0	3.747	2.042	0.7642	0.7488	1.9851
PC-I	2,000*	3.484 ^a	2.505 ^{ad}	0.8444	0.9186 ^{ad}	2.2047 ^a
PC-II	5,000*	3.783	2.435 ^d	0.9234 ^{bd}	0.9348 ^{bd}	2.1066
PC-III	20,000*	3.904	2.692 ^{bd}	1.0628 ^{bd}	1.0817 ^{bd}	2.1967 ^a
T-I	2,000	3.595	2.262	0.7865	0.8018	1.9377
T-II	5,000	3.890	2.460 ^d	0.8667	0.8916 ^c	2.1007
T-III	20,000	4.262 ^b	2.781 ^{bd}	1.0581 ^{bd}	1.0719 ^{bd}	2.3591 ^{bc}
						1.6458 ^{bd}

^a STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-I.

^b STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 99 PERCENT CONFIDENCE LEVEL FROM CONTROL-I.

^c STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

^d STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 99 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

* LEAD CARBONATE

TABLE XVII
TEST MATERIAL - PHENOL CHROMATE YELLOW
90-DAY SUBACUTE ORAL TOXICITY STUDY - ALBINO RATS

FJAL, SACRIFICE

ORGAN WEIGHT AND RATIO DATA

SUMMARY OF MEAN VALUES

ORGAN - LIVER

GROUP	DIETARY LEVEL (PPM)	ORGAN WEIGHT (GM)		ORGAN/BODY WEIGHT RATIO (GM/100 GM)		ORGAN/BRAIN WEIGHT RATIO (GM/GM)	
		MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
CONTROL-I	0	14.637	8.732	3.3141	3.1300	8.0404	5.2259
CONTROL-II	0	17.279 ^a	9.014	3.5129	3.3068	9.1538	5.0692
PC-I	2,000*	16.102	9.387	3.5675	3.4319	8.9135	5.5634
PC-II	5,000*	14.873	8.905	3.6228 ^a	3.4361	8.2901	5.1923
PC-III	20,000* 13.285 ^{cd}		8.378	3.6100 ^a	3.3622	7.4916 ^c	4.9675
T-I	2,000	15.085	9.457	3.2871	3.3491	8.1197	5.3654
T-II	5,000	15.707	9.447	3.5003	3.4079	8.4850	5.4282
T-III	20,000	14.499 ^c	9.237	3.5857	3.5439 ^b	8.0114	5.4754

^a STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-I.

^c STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

^d STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 99 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

* LEAD CARBONATE

TABLE XVIII
TEST MATERIAL - PHENOL CHROME YELLOW
90-DAY SUBACUTE ORAL TOXICITY STUDY - ALBINO RATS

FINAL SACRIFICE

ORGAN WEIGHT AND RATIO DATA

SUMMARY OF MEAN VALUES

ORGAN - SPLEEN

GROUP	DIETARY LEVEL (PPM)	ORGAN WEIGHT (GM)		ORGAN/BODY WEIGHT RATIO (GM/100 GM)		ORGAN/BRAIN WEIGHT RATIO (GM/GM)	
		MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
CONTROL-I	0	0.710	0.453	0.1677	0.1625	0.3933	0.2704
CONTROL-II	0	0.707	0.468	0.1429	0.1712	0.3728	0.2624
PC-I	2,000*	0.722	0.501	0.1601	0.1837	0.3999	0.2963
PC-II	5,000*	0.716	0.575 ^{ac}	0.1766	0.2218 ^{bc}	0.3999	0.3347 ^c
PC-III	20,000*	0.758	0.665 ^{bd}	0.2066 ^{bd}	0.2663 ^{bd}	0.4269	0.3946 ^{ad}
T-I	2,000	0.702	0.458	0.1545	0.1625	0.3791	0.2593
T-II	5,000	0.682	0.474	0.1522	0.1710	0.3679	0.2718
T-III	20,000	0.663	0.485	0.1640	0.1855	0.3658	0.2873

^a STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-I.

^b STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 99 PERCENT CONFIDENCE LEVEL FROM CONTROL-I.

^c STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 95 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

^d STATISTICALLY SIGNIFICANT DIFFERENCE AT THE 99 PERCENT CONFIDENCE LEVEL FROM CONTROL-II.

* LEAD CARBONATE

TABLE XIX
TEST MATERIAL - PRIMROSE CHROME YELLOW
90-DAY SUBCUTANEOUS ORAL TOXICITY STUDY - ALBINO RATS

FINAL SACRIFICE

ORGAN WEIGHT AND RATIO DATA

SUMMARY OF MEAN VALUES

ORGAN - THYROID GLAND

GROUP	INITIAL WEIGHT (G)	ORGAN WEIGHT (G)		ORGAN/BODY WEIGHT RATIO (GM/100 GM)		ORGAN/BRAIN WEIGHT RATIO (GM/GM)	
		MALES	FEMALES	MALES	FEMALES	MALES	FEMALES
CONTROL-I	0	0.022	0.021	0.0050	0.0077	0.0120	0.0126
CONTROL-II	0	0.025	0.025	0.0052	0.0093	0.0133	0.0141
PC-I	2,000*	0.027	0.023	0.0048	0.0085	0.0119	0.0137
PC-II	5,000*	0.025	0.022	0.0062	0.0084	0.0140	0.0127
PC-III	20,000*	0.024	0.023	0.0068	0.0093	0.0138	0.0136
T-I	2,000	0.025	0.024	0.0058	0.0086	0.0140	0.0136
T-II	5,000	0.024	0.025	0.0054	0.0091	0.0130	0.0143
T-III	20,000	0.024	0.025	0.0060	0.0096	0.0132	0.0146

NO STATISTICALLY SIGNIFICANT DIFFERENCES WERE NOTED.

* LEAD CARBONATE

3. Tissue Analyses

The results of the analyses of the liver, kidney, brain and bone for lead and chromium content are presented in Tables XX and XXI. The lead content of the bone, brain, kidney, and liver tissues was markedly increased in all animals fed either lead carbonate or Light Chrome Yellow. The greatest concentration of lead was in the bone samples. The lead content was increased in a dose-related manner.

Chromium content of the brain was increased only among the males fed 5,000 (PC-II) or 20,000 ppm (PC-III) of lead carbonate. This increase in brain chromium content among the PC-II and PC-III males was due to detectable amounts of chromium in the brain tissue of 2 of the 5 PC-II (5,000 ppm) animals and in the brain tissue of 1 of the 5 PC-III (20,000 ppm) animals. There was no chromium detectable in the brain tissue from the males and females fed 2,000 ppm (PC-I), from the females fed 5,000 ppm (PC-II), or from the females fed 20,000 ppm (PC-III) of lead carbonate. The bone, kidney, and liver chromium content of the animals fed lead carbonate was either comparable to or less than that of the control animals. Brain chromium content was increased among the males fed 2,000 ppm (T-I) or 20,000 ppm (T-III) Primrose Chrome Yellow. A slight increase in chromium content was noted among females fed 20,000 ppm (T-III) Primrose Chrome Yellow. There were no detectable amounts of chromium in the brain tissue from males fed 5,000 ppm (T-II) or from females fed 2,000 (T-I) or 5,000 ppm (T-II).

The bone chromium content was increased among males fed Primrose Chrome Yellow (T-I, T-II, and T-III) and among females fed 5,000 (T-II) or 20,000 ppm (T-III). Kidney and liver chromium content was increased in all groups (T-I, T-II, and T-III) fed Primrose Chrome Yellow. The increases in chromium content were generally dose-related.

TABLE XX
TEST MATERIAL: Primrose Chrome Yellow
90 Day Subacute Oral Toxicity Study - Albino Rats

Tissue Analyses

Summary of Mean Values - Males

Group and Dietary Level (ppm)	Lead Content (µg/g)			Chromium Content (µg/g)		
	Bone	Brain	Kidney	Liver	Bone	Brain
Control I (0)	0.44	ND	0.164	0.013	0.188	ND
Control II (0)	0.24	0.018	0.066	0.022	0.277	ND
PG I (2,000)*	108	0.401	13.7	0.55	ND	ND
PG II (5,000)*	220	0.765	26.5	2.37	ND	0.314 ^a
PG III (20,000)*	481	1.32	30.7	4.36	ND	0.308 ^b
I I (2,000)	53	0.557	10.8	2.13	0.448	0.189
I II (5,000)	93	0.259	17.7	1.73	0.572	ND
I III (20,000)	363	1.25	68.2	3.93	1.47	0.127
						2.36
						0.075
						0.058
						0.086
						0.072
						0.086
						0.403
						0.286
						1.02

ND = (Not detectable) Less than detection limit: Pb 0.001 µg/g
Cr 0.010 µg/g Brain
0.050 µg/g Bone, Liver, and Kidney

* = Detection of Cr in 2 of 5 animals.

b = Detection of Cr in 1 of 5 animals.

* Lead Carbonate

TABLE XXI

TEST MATERIAL: Polynuclear Chromene Yellow

90-Day Subacute Oral Toxicity Study - Albino Rats

Tissue Analyses

Summary of Mean Values - Females

Group and Dietary Level (ppm)	Lead Content (µg/g)			Chromium Content (µg/g)		
	Bone	Brain	Kidney	Bone	Brain	Kidney
Control I (0)	0.85	0.518	0.670	0.336	ND	ND
Control II (0)	0.22	0.401	0.199	0.280	ND	ND
PC I (2,000)*	128	0.565	23.9	ND	ND	ND
PC II (5,000)*	236	0.674	33.3	ND	ND	ND
PC III (20,000)*	540	0.974	34.7	ND	ND	ND
T-I (2,000)	52	0.114	10.1	ND	ND	0.491
T-II (5,000)	108	0.365	24.0	0.844	ND	0.945
T-III (20,000)	250	0.876	55.4	1.36	0.076	4.33
						1.07

ND : (Not detectable) Less than detection limit: Pb 0.001 µg/g Brain
 Cr 0.010 µg/g Bone, Liver, and Kidney
 0.050 µg/g Bone, Liver, and Kidney

* Lead Carbonate

4. Histopathologic Findings

Histopathologic examination of tissues and organs from Control-I, Control-II, PC-III (20,000 ppm) and T-III (20,000 ppm) groups sacrificed after 90 days of testing presented in Tables XXII and XXIII. Individual treatment-related kidney findings (Tables XXIV and XXV) and incidental kidney findings (Tables XXVI and XXVII) are presented for each group of animals.

The pathologist's statement is presented on the next page.

I. B. T. Study Number 622-05921C
Dry Color Manufacturers' Association

A histopathological examination was conducted on a series of tissues from rats of the untreated control groups (C-I, C-II), positive control group (PC-III), and high dose test group (T-III) of I. B. T. Study Number 622-05921C. Subsequently, sections of both kidneys were examined from all animals from the other positive control groups (PC-I, PC-II) and the other test groups (T-I, T-II). Animals in positive control groups were fed 3 different levels of lead carbonate while the test animals were fed comparable levels of Primrose Chrome Yellow.

Several different treatment-related effects occurred in the kidney. They consisted of tubular epithelial cell alterations, an associated increased incidence and severity of focal interstitial lymphocytic cell infiltrates, and chronic nephritis.

Treatment-related renal lesions consisting of tubular epithelial cell alterations were present among almost all animals of the 3 positive control groups (lead carbonate), and they are tabulated in Tables XXIV and XXV. These changes were most prominent and confined to tubules located in the mid and inner segments of the cortex.

The treatment-related tubular epithelial cell effects consisted of:

- 1) Hypertrophy (enlargement) of epithelial cells lining the tubules. The enlargement of these cells was due to an increase in both the cytoplasmic and nuclear masses. The nuclei of these cells were enlarged and pleomor-

phic in appearance with multiple enlarged nucleoli. The nuclei of some of these cells also contained inclusion bodies which were oval to round, homogenous and eosinophilic in H & E stained sections.

2) Desquamation of degenerate or necrotic cells into the lumen of the affected tubules.

3) Increased number of mitotic figures in the nuclei of tubular epithelial cells in the affected regions.

The incidence of these lesions was similar among all of the positive control groups. However, the relative severity was most severe among animals in the PC-III level and was considered dose-related.

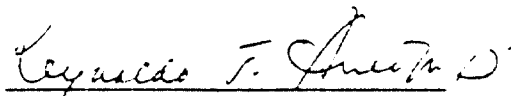
Similar treatment-related renal lesions were present among almost all T-I, T-II, and T-III animals fed Primrose Chrome Yellow. The renal tubular lesions were more pronounced in the T-III group, but there were no increased numbers of mitotic figures as noted with lead carbonate. The relative severity (and extent) of these changes among animals fed Primrose Chrome Yellow were not as severe as they were among animals fed with comparable levels of lead carbonate.

The other treatment-related renal effects consisted of focal interstitial lymphocytic cell infiltrations and chronic nephritis. These changes were present among the untreated control, positive control and test animals. In the untreated control groups, focal interstitial lymphocytic

cell infiltrations were often located unilaterally and were unrelated to the treatment-related tubular changes described above. Among almost all of the positive control animals and most of the T-III animals, focal interstitial lymphocytic cell infiltrations were often located bilaterally and were associated with treatment-related tubular changes described above. Although chronic nephritis was present among control, positive control, and test animals, the highest incidence occurred among the PC-III males and females. The increased incidence and location of chronic nephritis among the PC-III animals was associated with the more severe tubular changes observed among this group of animals.

In general, all of the treatment-related renal tubular epithelial lesions were dose-related, and they were most pronounced among the positive control animals. Similar, but less severe, lesions were present among the test animals. Several lesions of naturally occurring diseases (focal interstitial lymphocytic cell infiltrations and chronic nephritis) were augmented in the positive control and test animals.

The other changes described in the kidney and other tissues are regarded as lesions of naturally occurring diseases, or related to the method of sacrifice. In most instances, these changes were present in all groups of animals.


Reynaldo J. Arceo, M.D.
Staff Pathologist

Reviewed and Approved:

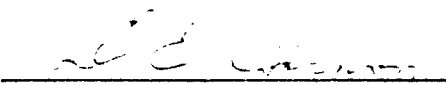

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TABLE XXII
TEST MATERIAL: P-Increase Chrome Yellow
90 Day Subacute Oral Toxicity Study - Allomo Rats

Final Sacrifice

Summary of Histopathologic Findings - Males

Organ	Findings	Control I			Control II (0)			Positive Control III (20,000 ppm)*			T-III (20,000 ppm)		
		Incidence	Average Grade	20	Incidence	Average Grade	20	Incidence	Average Grade	20	Incidence	Average Grade	20
Adrenal glands	Bilateral, focal lipomatous degeneration of cortex	1	1.5	2	1.0			0			0		
	Bilateral, diffuse lipomatous degeneration of cortex	1	2.5	1	2.0			0			0		
Colon	Parasites in lumen (Nematodiasis)	5	P	1	P			0			1	P	
Eyes	Bilateral, focal chronic chorioiditis	2	1.5	0				0			0		
	Unilateral retinal degeneration	0		0				1	1.0		0		
	Unilateral, focal, chronic dacryoadenitis	0		0				0			0		
Heart	Multifocal, chronic epicarditis and myocarditis	2	2.5	0				0			0		
	Focal, chronic myocarditis	2	1.0	2	1.0			1	1.0		7	1.1	
	Multifocal, chronic myocarditis	2	2.5	0				0			0		
	Focal fibrosis	0		0				1	1.0		0		
Liver	Focal, extramedullary hematopoiesis	5	1.0	3	1.0			5	1.0		3	1.0	
	Focal, cytoplasmic vacuolation (lipids)	2	1.2	2	1.2			0			1	1.0	
	Multifocal, cytoplasmic vacuolation (lipids)	1	2.5	0				0			0		
	Small focus of necrotic hepatitis	1	1.0	0				0			0		
	Abscess	1	2.0	0				0			0		
	Focal bile duct proliferation	0		0				1	1.0		0		

TABLE XXII continued

TEST MATERIAL: Primrose Chrome Yellow

90 Day Subacute Oral Toxicity Study - Albino Rats

Final Sacrifice

Summary of Histopathologic Findings - Males

Organ	Findings	Group:		Control I		Control II		Positive Control III		T III	
		Dietary Level:	Number Examined:	(0)		(0)		(20,000 ppm)*		(20,000 ppm)	
				Incidence	Average Grade	Incidence	Average Grade	Incidence	Average Grade	Incidence	Average Grade
Lungs	Chronic murine pneumonia		16	1.7	20	1.4	19	1.4	20	1.6	
	Focal aggregates of alveolar macrophages		6	1.0	6	1.1	2	1.2	3	1.0	
	Acute, multifocal fibrino-necrotic bronchopneumonia		2	3.0	0	-	0	-	0	-	
	Focal congestion (agonal)		0	-	0	-	0	-	1	2.0	
	Focal hemorrhage (agonal)		3	1.7	0	-	0	-	0	-	
	Focal edema		1	2.0	0	-	0	-	0	-	
Pituitary gland	Focal, chronic bronchopneumonia		0	-	1	1.0	0	-	0	-	
	Focal, cytoplasmic vacuolation (lipids)		0	-	0	-	1	1.0	0	-	
Prostate gland	Focal, interstitial lymphoid infiltrations		1	2.0	3	1.0	1	1.0	2	1.0	
Spleen	Increased extramedullary hematopoiesis		5	1.4	3	1.3	7	1.5	4	1.0	
Testes	Bilateral, diffuse testicular degeneration with mineralization of some seminiferous tubules		1	3.0	1	3.5	0	-	0	-	
	Bilateral, focal testicular degeneration		0	-	0	-	1	1.5	0	-	
Trachea	Focal, chronic tracheitis		0	-	0	-	3	1.3	0	-	
Urinary bladder	Proteinaceous plug in lumen		10	1.0	11	1.0	12	1.0	12	1.0	

Grading System:

- 1.0 = Minimal or trace
 2.0 = Mild in severity
 3.0 = Moderate in severity
 4.0 = Marked in severity
 5.0 = Extreme in severity

P = Present

* Lead Carbonate

TABLE XXIII

TEST MATERIAL: Primrose Chrome Yellow

90 Day Subacute Oral Toxicity Study - Albino Rats

Final Sacrifice

Summary of Histopathologic Findings - Females

Organ	Findings	Control-I (0) 20			Control-II (0) 20			Positive Control-III (20,000 ppm)* 20			T-III (20,000 ppm) 20		
		Incidence	Average Grade	Number Examined	Incidence	Average Grade	Number Examined	Incidence	Average Grade	Number Examined	Incidence	Average Grade	Number Examined
Adrenal glands	Bilateral, focal, lipomatous degeneration of cortex	1	1.0	0	0	-	0	0	-	0	0	-	0
Carcin	Parasites in lumen (Nematodiasis)	1	P	1	P	-	0	0	-	0	0	-	0
Colon	Parasites in lumen (Nematodiasis)	4	P	0	0	-	0	0	-	1	P	-	1
Eyes	Unilateral, focal, chronic dacryoadenitis	1	1.0	0	0	-	0	0	-	1	1.0	-	1
	Chronic, diffuse choroiditis with adhesions to posterior lens capsule and mineralization of lens	0	-	0	0	-	0	0	-	1	2.0	-	1
Heart	Focal, chronic myocarditis	0	-	1	1.0	-	2	1.0	-	0	0	-	0
Liver	Focal, extramedullary hematopoiesis	4	1.1	4	1.0	-	5	1.0	-	3	1.0	-	3
	Focal, cytoplasmic vacuolation (lipids)	2	1.2	0	0	-	0	0	-	0	0	-	0
	Bile duct proliferation	0	-	0	0	-	1	1.0	-	0	0	-	0
Lungs	Chronic murine pneumonia	19	1.4	20	1.2	-	19	1.4	-	16	1.1	-	16
	Focal aggregates of alveolar macrophages	6	1.0	2	1.2	-	3	1.2	-	2	1.0	-	2
	Focal hemorrhage (agonal)	2	1.2	2	2.0	-	0	0	-	0	0	-	0
	Congestion (agonal)	1	3.0	2	2.8	-	3	2.5	-	3	0	-	3
	Focal, acute bronchopneumonia	0	-	0	0	-	1	1.0	-	1	0	-	1

TABLE XXIII continued

TEST MATERIAL: Priarose Chrome Yellow

90 Day Subacute Oral Toxicity Study Albino Rats

Final Sacrifice

Summary of Histopathologic Findings - Females

Summary of Histopathologic Findings											
Organ	Findings	Group: Dietary Level: Number Examined:		Control-I (0) 20		Control-II (0) 20		Positive Control-III (20,000 ppm)* 20		T III (20,000 ppm) 20	
		Incidence	Average Grade	Incidence	Average Grade	Incidence	Average Grade	Incidence	Average Grade	Incidence	Average Grade
Spleen	Increased extramedullary hematopoiesis	2	1.0	2	1.0	9	1.3	2	1.0		
	Increased hemosiderin pigment	0	-	0	-	1	1.0	0	-		
Trachea	Focal, chronic tracheitis	0	-	1	1.0	2	1.0	1	1.0		
Uterus	Hydrometra	3	1.5	1	1.5	1	1.0	3	1.2		
	Suppurative metritis	1	1.0	1	1.0	2	1.0	3	1.0		
	Subacute, focal cervicitis	1	1.0	0	-	0	-	0	-		

Grading System:

1.0 - Minimal or trace

2.0 - Mild to severity

3.0 - Moderate to severity

4.0 - Marked to severity

5.0 - Extreme to severity

P - Present

* Lead Carbonate

TABLE XXIV

TEST MATERIAL: Primrose Chrome Yellow

90-Day Subacute Oral Toxicity Study - Albino Rats

Treatment-Related Histopathologic Effects - Males

Microscopic Renal Lesions

Group Dietary Level (ppm)	Animal Number and sex	Tubular Changes			Mitotic Figures	Focal Interstitial Lymphoid Infiltrations ^{a,b}	Chronic Nephritis ^{a,b}
		Hypertrophy of cells	Intranuclear Inclusions	Desquamated Cells in Lumen			
Control-I (0)	1-M					• (U)	
	2-M					• (U)	
	3-M						
	4-M					• (U)	
	5-M						
	6-M						
	7-M					• (U)	
	8-M					•	• to • (U)
	9-M					•	
	10-M						
	11-M					• to •	
	12-M						
	13-M					•	
	14-M						
	15-M					•	
	16-M						
	17-M					• (U)	
	18-M						
	19-M					•	
	20-M					• (U)	
Control-II (0)	41-M					•	
	42-M						
	43-M						
	44-M					• (U)	
	45-M					•	
	46-M						
	47-M					• (U)	
	48-M					• to •	
	49-M						
	50-M					•	
	51-M						
	52-M					• (U)	
	53-M					• (U)	
	54-M						
	55-M					•	
	56-M						
	57-M						
	58-M						
	59-M						
	60-M					• (U)	• (U)

a All lesions are bilateral unless otherwise indicated.

b All lesions are focal unless otherwise indicated.

(U) Unilateral

• = Minimal or trace

•• = Mild in severity

••• = Moderate in severity

TABLE XXV continued

TEST MATERIAL: Primrose Chrome Yellow
 90-Day Subacute Oral Toxicity Study - Albino Rats
 Treatment-Related Histopathologic Effects - Males
 Microscopic Renal Lesions

Group Dietary Level (ppm)	Animal Number and Sex	Tubular Changes Hypertrophy of Cells	Intranuclear Inclusions	Desquamated Cells in Lumen	Mitotic Figures	Focal Interstitial Lymphoid Infiltrations ^{a,b}	Chronic Nephritis ^{a,b}
PC-I (2,000) ^a	81-M	- to -	+	+		+	
	82-M	-		+		+	
	83-M	+ to -	+			+	
	84-M	-	+			+	
	85-M	+ to -	+	-		+	
	86-M	-	-			- to -	
	87-M	-	-			+	
	88-M	- to -	+	+		+	
	89-M	-	+	-		+	
	90-M	+ to -	+	-		+	
PC-II (5,000) ^a	121-M	-	-	-		+	
	122-M	-	-	- to -		- to -	
	123-M	-	+	+		+	
	124-M	-	-	+		+	
	125-M	- to -	- to -	+		+	
	126-M	-	-	+		+	
	127-M	-	-	+		+	
	128-M	- to -	-	+		+	
	129-M	- to -	- to -	+		+	
	130-M	-	-	+		+	
PC-III (20,000) ^a	161-M	-	+	+		- to -	+
	162-M	+	-	+		+	
	163-M	-	-	+		+	
	164-M	-	-	+	- to -	+	
	165-M	-	-	+		- to -	- (U)
	166-M	- to -	-	+		+	- (U)
	167-M	-	- to -	+		+	+
	168-M	+	-	+		+	- (M)
	169-M	- to -	- to -	- to -		+	
	170-M	-	- to -	+		+	
	171-M ⁼⁼	-	-	+		- to -	
	172-M	- to -	-	+		+	
	173-M	- to -	-	+		+	- to -
	174-M	- to -	+	+		+	- (M)
	175-M	- to -	-	+		+	
	176-M	- to -	-	+		+	
	177-M	-	-	+		+	
	178-M	- to -	-	+		+	
	179-M	-	+	+		+	- (M)
	180-M	-	+	+		+	

^a All lesions are bilateral unless otherwise indicated.
^b All lesions are focal unless otherwise indicated.

(U) Unilateral
 (M) Multifocal

- Lead Carbonate
 == Postmortem animal.

Industrial BIO-TEST Laboratories, Inc.

TABLE XXX continued

TEST MATERIAL Primrose Chrome Yellow
 90-Day Subacute Oral Toxicity Study - Albino Rats
 Treatment-Related Histopathologic Effects - Males

Microscopic Renal Lesions

Group Dietary Level (ppm)	Animal Number and Sex	Tubular Changes Hypertrophy of Cells	Intranuclear Inclusions	Desquamated Cells in Lumen	Mitotic Figures	Focal Interstitial Lymphoid Infiltrations ^{a,b}	Chronic Nephritis ^{a,b}
T-I (2,000)	441-M	+ to ++					
	442-M	+ to ++	•				
	443-M	•					
	444-M	•					
	445-M	+ to ++					
	446-M	•					
	447-M	•					
	448-M	•					
	449-M	+ to ++	•				
	450-M	•					
T-II	481-M	+ to ++	•	•			
	482-M	•	•	•			
	483-M	+ to ++	•	•			
	484-M	•	•	•			
	485-M	+ to ++	•	•			
	486-M	+ to ++	•	•			
	487-M	•	•	•			
	488-M	•	•	•			
	489-M	+ to ++	•	•			
	490-M	+ to ++	•	•			
T-III (20,000)	521-M	•					
	522-M	•	•	•		•	
	523-M	+ to ++	•	•		•	
	524-M	•	•	•		+ to ++	
	525-M	+ to ++	•	•		•	
	526-M	•	•	•		•	
	527-M	+ to ++	•	•		•	
	528-M	•	•	•		•	
	529-M	+ to ++	•	•		•	
	530-M	•	•	•		•	
	531-M	+ to ++	•	•		•	
	532-M	+ to ++	•	•		•	
	533-M	•	•	•		•	
	534-M	+ to ++	•	•		•	
	535-M	•	•	•		•	
	536-M ^a	+ to ++	•	•		+ to ++	•
	537-M	•	•	•		•	
	538-M	•	•	•		•	
	539-M	+ to ++	•	•		•	
	540-M	•	•	•		•	

* Postmortem animal.

a All lesions are bilateral unless otherwise indicated.

b All lesions are focal unless otherwise indicated.

c Unilateral.

TABLE XXV

TEST MATERIAL: Primrose Chrome Yellow

90-Day Subacute Oral Toxicity Study - Albino Rats

Treatment-Related Histopathologic Effects - Females

Microscopic Renal Lesions

Group Dietary Level (ppm)	Animal Number and Sex	Tubular Changes Hypertrophy of Cells	Intranuclear Inclusions	Desquamated Cells in Lumen	Mitotic Figures	Focal Interstitial Lymphoid Infiltrations ^{a, b}	Chronic Nephritis ^{a, b}
Control-I (0)	21-F						
	22-F						
	23-F						
	24-F						
	25-F						
	26-F						
	27-F					-	
	28-F					-	
	29-F						
	30-F						
	31-F					-	
	32-F					+ (U)	
	33-F						
	34-F						
	35-F						
	36-F						
	37-F					+ to -- (U)	
	38-F**						
	39-F						
	40-F						
Control-II (0)	51-F						
	52-F						
	53-F					+ (U)	
	54-F						
	55-F					- (U)	
	56-F						
	57-F					+ (U)	
	58-F						
	59-F						
	60-F						
	61-F						
	62-F						
	63-F						
	64-F						
	65-F						
	66-F						
	67-F						
	68-F						
	69-F						
	70-F						
	71-F					+ to -- (U)	
	72-F						
	73-F						
	74-F						
	75-F						
	76-F						
	77-F						
	78-F						
	79-F						
	80-F					- (U)	

^a All lesions are bilateral unless otherwise indicated.^b All lesions are focal unless otherwise indicated.

(U) Unilateral

- = Minimal or trace

-- = Mild in severity

--- = Moderate in severity

** Postmortem animal

TABLE XXV continued

TEST MATERIAL: Primrose Chrome Yellow

90-Day Subacute Oral Toxicity Study - Albino Rats

Treatment-Related Histopathologic Effects - Females

Microscopic Renal Lesions

Group Dietary Level (ppm)	Animal Number and Sex	Tubular Hypertrophy of Cells	Changes Intranuclear Inclusions	Desquamated Cells in Lumen	Mitotic Figures	Focal Interstitial Lymphoid Infiltrations ^{a,b}	Chronic Nephritis ^{a,b}
PC-I (2,000) ^a	101-F	-	+			+	(U)
	102-F	-	+				
	103-F	- to --	+				
	104-F	- to --	+	+			
	105-F	--	+				
	106-F	-	+				
	107-F	- to --	+	+			
	108-F	-	+				
	109-F	-	- to --				
	110-F	- to --	+	+			
PC-II (5,000) ^a	141-F	- to --	--				
	142-F	- to --	--				
	143-F	--	--	+			
	144-F	- to --	- to --				
	145-F	--	--				
	146-F	--	--	-		- to --	
	147-F	--	- to --				
	148-F	--	--			- to --	
	149-F	--	--				
	150-F	- to --	-				
PC-III (20,000) ^a	181-F	- to --	--				- to --
	182-F	-	- to --	-			
	183-F	-	- to --				- (U)
	184-F	- to --	--				
	185-F	-	--			- (U)	
	186-F	- to --	--	+			
	187-F ⁼⁼		- to --				
	188-F	- to --	--	-			
	189-F ⁼⁼	-	- to --	-		- to --	
	190-F ⁼⁼	-	-				
	191-F ⁼⁼	-		-			- to -- (34)
	192-F ⁼⁼						
	193-F ⁼⁼						
	194-F ⁼⁼	- to --					
	195-F ⁼⁼	-					
	196-F ⁼⁼	- to --	- to --				
	197-F	--	--	-			
	198-F	--	--	-		- to --	
	199-F	-	- to --				
	200-F	- to --	- to --	-			

^a All lesions are bilateral unless otherwise indicated.^b All lesions are focal unless otherwise indicated.

(U) Unilateral

(M) Multifocal

* Lead Carbonate

== Postmortem animal

Industrial BIO-TEST Laboratories, Inc.

TABLE XXV continued

TEST MATERIAL: Primrose Chrome Yellow
 90-Day Subacute Oral Toxicity Study - Albino Rats
 Treatment-Related Histopathologic Effects - Females

Microscopic Renal Lesions

Group Dietary Level (ppm)	Animal Number and Sex	Tubular Changes Hypertrophy of Cells	Intranuclear Inclusions	Desquamated Cells in Lumen	Mitotic Figures	Focal Interstitial Lymphoid Infiltrations ^{a,b}	Chronic Nephritis ^{a,b}
T-I (2,000)	461-F	-	-	-	-	-	-
	462-F	-	-	-	-	-	-
	463-F	-	-	-	-	-	-
	464-F	-	-	-	-	-	-
	465-F	-	-	-	-	-	-
	466-F	-	-	-	-	-	-
	467-F	-	-	-	-	-	-
	468-F	-	-	-	-	-	-
	469-F	-	-	-	-	-	-
	470-F	-	-	-	-	-	-
T-II (5,000)	501-F	- to ++	-	-	-	-	-
	502-F	-	-	-	-	-	-
	503-F	- to ++	-	-	-	-	-
	504-F	- to ++	-	-	-	-	-
	505-F	-	-	-	-	-	-
	506-F	- to ++	-	-	-	-	-
	507-F	- to ++	-	-	-	-	-
	508-F	-	-	-	-	-	-
	509-F	- to ++	-	-	-	-	-
	510-F	- to ++	-	-	-	-	-
T-III (20,000)	541-F	- to ++	-	-	-	-	-
	542-F	- to ++	- to ++	-	-	-	-
	543-F	- to ++	-	-	-	-	-
	544-F	-	-	-	-	-	-
	545-F	-	-	-	-	-	-
	546-F ^a	-	Evaluation Precluded by Autolysis			-	-
	547-F	-	-	-	-	-	-
	548-F ^a	-	Evaluation Precluded by Autolysis			-	-
	549-F	- to ++	-	-	-	- to ++	-
	550-F	-	- to ++	-	-	-	-
	551-F	-	-	-	-	-	-
	552-F ^a	- to ++	-	-	-	- to ++	-
	553-F	-	-	-	-	-	-
	554-F	-	-	-	-	-	-
	555-F	- to ++	-	-	-	- (U)	-
	556-F	- to ++	-	-	-	-	-
	557-F	- to ++	- to ++	-	-	-	-
	558-F	- to ++	-	-	-	-	-
	559-F	- to ++	-	-	-	-	-
	560-F	-	-	-	-	-	-

* Postmortem animal.

a All lesions are bilateral unless otherwise indicated.

b All lesions are focal unless otherwise indicated.

U = Unilateral.

- Few scattered cells affected in entire section.

Industrial BIO-TEST Laboratories, Inc.

TABLE XXVI

TEST MATERIAL: Primrose Chrome Yellow

90 Day Subacute Oral Toxicity Study - Albino Rats

Final Sacrifice

Incidental Kidney Findings - Males																			
Organ	Findings	Group		Control I		Control II		PC-I (2,000)*		PC-II (5,000)*		PC-III (20,000)*		T-I (2,000)		T-II (5,000)		T-III (20,000)	
		Dietary Level (ppm)		(0)		(0)		20		10		20		10		10		20	
		Avg.	Gr.	Avg.	Gr.	Avg.	Gr.	Avg.	Gr.	Avg.	Gr.	Avg.	Gr.	Avg.	Gr.	Avg.	Gr.	Avg.	Gr.
Kidneys	Bilateral, mineralized microconcretions in tubules	1	1.5	4	1.0	3	1.0	1	1.0	1	1.0	1	1.0	0	0	0	0	2	1.0
	Unilateral, mineralized microconcretions in tubules	2	1.0	7	1.0	2	1.0	1	1.0	2	1.0	2	1.0	1	1.0	0	0	6	1.0
	Unilateral hydronephrosis	2	1.0	0	0	0	0	0	0	0	0	1	2.0	0	0	0	0	0	0
	Bilateral, local, proteinaceous tubular casts	1	1.0	1	1.0	0	0	0	0	0	0	1	1.0	0	0	0	0	0	0
	Unilateral, local, proteinaceous tubular casts	0	0	1	1.0	0	0	0	0	0	0	2	1.0	0	0	0	0	0	0
	Bilateral, tubular nephrosis	4	1.6	3	1.2	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Unilateral, tubular nephrosis	2	1.0	2	1.0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Unilateral, pyelonephritis	1	1.0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
	Unilateral, pyelonephritis	1	1.0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0

Grading System:

1.0 - Minimal or trace

2.0 - Mild to severity

3.0 - Moderate to severity

4.0 - Marked to severity

5.0 - Extreme to severity

P - Present

Key:

I - Incidence

Avg. Gr. - Average Grade

* Lead Carbonate

TABLE XXVII

Prinsep Chrome Yellow

Day Subacute Oral Toxicity Study · Allomo Ratio

Personal Sacrifice

Incidental Kidney Findings - Females																	
	Group	Control I (0)		Control II (0)		PC I (2,000)*		PC II (5,000)*		PC III (20,000)		T-I (2,000)		T-II (5,000)		T-III (20,000)	
		Dietary Level (ppm) Nodules Examined		Avg.	Gr.	Avg.	Gr.	Avg.	Gr.	Avg.	Gr.	Avg.	Gr.	Avg.	Gr.	Avg.	Gr.
		I	Gr.	I	Gr.	I	Gr.	I	Gr.	I	Gr.	I	Gr.	I	Gr.	I	Gr.
Findings																	
Groups	Bilateral, mineralized microconstrictions in tubules	5	1.0	6	1.0	1	1.0	3	1.0	8	1.0	0	-	0	-	0	-
	Unilateral, mineralized microconstrictions in tubules	5	1.0	5	1.0	1	1.0	0	-	3	1.0	0	-	0	-	0	-
Findings	Bilateral, focal, proteinaceous tubular casts	0	0	0	0	0	0	0	0	2	1.0	0	-	0	-	0	-
	Unilateral, focal, proteinaceous tubular casts	0	0	1	1.0	0	0	0	0	1	1.0	0	-	0	-	0	-
	Bilateral, tubular nephrosis	0	0	2	1.0	0	0	0	0	0	0	0	-	0	-	0	-
	Unilateral, tubular nephrosis	0	0	2	1.0	0	0	0	0	0	0	0	-	0	-	0	-

$\text{C}_{60}\text{H}_8\text{N}_2$

Approved for Release

Agencies in Italy

Could in reality
be made in reality

Abolition in slavery

Marked in severity

6,980,000 100

we infer

64 - Average Grade

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Triage of 8(e) Submissions

Date sent to triage: _____

NON-CAP

CAP

Submission number: 12317A

TSCA Inventory:

Y

N

D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO

AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX

SBTOX

SEN

w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX

CTOX

EPI

RTOX

GTOX

STOX/ONCO

CTOX/ONCO

IMMUNO

CYTO

NEUR

Other (FATE, EXPO, MET, etc.): _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 pages 1,2 pages _____

Notes:

Contractor reviewer : JW Date: 1/17/96

CECATS DATA
Submission # BEHQ-1092-12317 SEQ. A

TYPE: INT. SUPP FLWP

SUBMITTER NAME: Ciba-Geigy
Corporation

INFORMATION REQUESTED: FLWP DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)
DISPOSITION:
0505 REFER TO CHEMICAL SCREENING
0506 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED (HUMAN)
0403 NOTIFICATION IN WORKING STATUS
0404 LABORATORY (TIAMIS)
0405 PROCESS/ANALYSIS (TIAMIS)
0406 APPRAISE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 10/19/92 OTS DATE: 10/20/92 CSRAD DATE: 03/27/95

CHEMICAL NAME:

Chromose Chrome yellow ~~none~~ none

CASE

1344-37-2

BEST COPY AVAILABLE

INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.	INFORMATION TYPE:	P.F.C.
0201 ONCO (HUMAN)	01 02 04	0216 EPICLIN	01 02 04	0241 IMMUNO (ANIMAL)	01 02 04
0202 ONCO (ANIMAL)	01 02 04	0217 HUMAN EXPOS (PROD CONTAM)	01 02 04	0242 IMMUNO (HUMAN)	01 02 04
0203 CELL TRANS (IN VITRO)	01 02 04	0218 HUMAN EXPOS (ACCIDENTAL)	01 02 04	0243 CHEMPHYS PROP	01 02 04
0204 MUTA (IN VITRO)	01 02 04	0219 HUMAN EXPOS (MONITORING)	01 02 04	0244 CLASTO (IN VITRO)	01 02 04
0205 MUTA (IN VIVO)	01 02 04	0220 BODILY TOX	01 02 04	0245 CLASTO (ANIMAL)	01 02 04
0206 REPRO/TERATO (HUMAN)	01 02 04	0221 ENV. OCCUREL/FATE	01 02 04	0246 CLASTO (HUMAN)	01 02 04
0207 REPRO/TERATO (ANIMAL)	01 02 04	0222 EMER INCI OF ENV CONTAM	01 02 04	<u>0247</u> DNA DAMREPAIR	01 02 04
0208 NEURO (HUMAN)	01 02 04	0223 RESPONSE REQUEST DELAY	01 02 04	0248 PRODUCE/PROC	01 02 04
0209 NEURO (ANIMAL)	01 02 04	0224 PRODUCE/CHEM ID	01 02 04	0251 MSDS	01 02 04
0210 ACUTE TOX. (HUMAN)	01 02 04	0225 REPORTING RATIONALE	01 02 04	0259 OTHER	01 02 04
0211 CHR. TOX. (HUMAN)	01 02 04	0226 CONFIDENTIAL	01 02 04		
0212 ACUTE TOX. (ANIMAL)	01 02 04	0227 ALLERG (HUMAN)	01 02 04		
<u>0213</u> SUB ACUTE TOX (ANIMAL)	01 02 04	0228 ALLERG (ANIMAL)	01 02 04		
0214 SUB CHRONIC TOX (ANIMAL)	01 02 04	0229 METAPHARMACO (ANIMAL)	01 02 04		
0215 CHRONIC TOX (ANIMAL)	01 02 04	0230 METAPHARMACO (HUMAN)	01 02 04		

IRADIATION NON-CL INVENTORY

YES

ONCOLOGIC REVIEW

YES (DROP/REFER)

SPECIES

RAT

TOXICOLOGICAL CONCERN

LOW

MED

HIGH

CAS SR

NO

NO (CONTINUE)

IN PLANN

REFR

USE:

Dye

PRODUCTION:

1:1000 Rats received lead sulfachromate at dietary concentrations of 2000, 5000 or 20000 ppm for 90 days. Dose-related effects included hemoglobin and hematocrit values, abnormal erythrocyte morphology. Microscopic changes included renal lesions, focal interstitial lymphocyte cell infiltrations. The NOAEL was not achieved. ~~The NOAEL was not achieved.~~